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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Paper No. 0204

Application Number: 09/818,990
Filing Date: March 27, 2001
Appellant(s): WALKE, ET AL.

mailed-date
03-03-04

David W. Hibler
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief in, filed on December 2, 2003.

***(1) Real Party in Interest***

A statement identifying the real party in interest is contained in the brief.

***(2) Related Appeals and Interferences***

Appellant's brief includes a statement that there are no related appeals or interferences.

***(3) Status of Claims***

The statement of the status of the claims contained in the brief is correct.

***(4) Status of Amendments After Final***

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

***(5) Summary of Invention***

The summary of invention contained in the brief is correct.

*(6) Issues*

The appellant's statement of the issues in the brief is correct.

*(7) Grouping of Claims*

Appellant's brief includes a statement that, regarding rejection of Claims 1-3 and 6-10 under 35 U.S.C. 101 and under 35 U.S.C. 112, first paragraph for lack of enablement, the claims stand or fall together. Regarding rejection of Claim 1 under 35 U.S.C. 112, first paragraph for insufficient written description, Appellant's brief state that Claim 1 will stand or fall alone. However, Claims 7 and 10, as dependent on Claim 1, were also rejected under 35 U.S.C. 112, first paragraph (see the First Action on the Merits of December 27, 2002). Said rejection of Claims 7 and 10, although not mentioned in the Final Rejection, was never withdrawn. Therefore, regarding rejection of Claims 1, 7, and 10 under 35 U.S.C. 112, first paragraph for insufficient written description, the claims will fall or stand together.

*(8) Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

***(9) Prior Art of Record***

1) Hillier L et al Genome Res. 6 (9): 807-828 1996 Genbank Acc# AA179499 Alignment with SEQ ID NO: 1.

2) Ausubel et al Current Protocols in Molecular Biology Chapter 16. Protein Expression. 1987 John Wiley & Sons, Inc.

3) Zheng XM, et al. Nature. 1990 Apr 5;344(6266):556-9. EMBL Acc# X53281. Alignment with Genbank Acc# AA179499 of Hillier et al. BLAST PRINT OUT.

4) Bork et al., Genome Research, vol. 10 (2000), pp. 398-400.

5) Smith et al., Nature Biotechnology, vol. 15 (1997), pp. 1222-1223.

6) Brenner, Trends Genetics, vol. 15 (1999), pp. 132-133.

7) Broun et al., Science, vol. 282 (1998), pp. 1315-1317.

8) Van de Loo et al., Proc. Natl. Acad. Sci., vol. 92 (1995), pp. 6743-6747.

9) Musco et al., Biochemistry. 1995 Jan 17;34(2):553-61.

10) Marth et al., Nat Genet., vol 27(4) (2001), pp. 371-2.

11) NCBI Single Nucleotide Polymorphism (2000).

12) Musco et al., Biochemistry. 1995 Jan 17;34(2):553-61.

13) Smith et al, Oxford Dictionary of Biochemistry and Molecular Biology, (2000)Oxford University Press, Oxford, England. pages 437 and 649.

***(10) Grounds of Rejection***

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 USC § 101***

Claims 1-3 and 6-10 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 1-3 and 6-10 are directed to isolated polynucleotides encoding a novel protein. The specification discloses that the claimed polynucleotides encode "proteins that share sequence similarity with mammalian membrane and structural proteins" (pg 1, lines 9-10). The specification further states that "The novel human proteins described... share structural similarity with *inter alia*, mammalian muscle proteins (myosin light chain kinase, telokin, IgG like C2 domains, motilin), and modifiers and anchors of thereof (pg 2, lines 1-5). The specification asserts that "The novel human nucleic acid sequences described herein, encode alternative proteins/open reading frames of 1,320, 376, 419, 401, 459, 570, 754, 1,045, 102, 144, 126, 184, 295, and 479 amino acids in length (myosin light chain/titin-like protein), SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, and 28 respectively" (pg 2, lines 6-11).

While the specification states that the claimed polynucleotides encode proteins having structural similarity with mammalian membrane and structural proteins as well as mammalian muscle proteins (myosin light chain kinase, telokin, IgG like C2 domains, motilin), and modifiers and anchors of thereof, this disclosure of structural similarity is not an assertion of function or utility. The specification contains NO assertion of the function(s) present in the claimed polynucleotide or the proteins encoded thereby. Furthermore, while the specification asserts that the claimed polynucleotides encode alternative proteins/open reading frames of various lengths (myosin light chain/titin-like proteins), the claimed invention does not meet the utility requirements for the following reasons.

Even assuming arguendo that the specification asserts that the claimed polynucleotides encode a polypeptide having myosin light chain (pg 2, line 9), myosin light chain kinase (pg 2, line 2), or titin activity, which assertion is not present, here is no experimental evidence to support the assertion that the claimed polynucleotides encode a polypeptide having the function of myosin light chain, myosin light chain kinase, or titin. The alleged asserted function for the claimed polynucleotides has been determined solely on the basis of structural similarity (i.e. sequence homology). The state of the art clearly teaches the unpredictability of assigning function based on sequence homology and acknowledges that, small changes can drastically change function. Bork et al, 2000, Smith et al, 1997 and Brenner, 1999 are some of the references that describe the overall state of the art in regard to the unpredictability of annotating function. Bork et al teaches the pitfalls associated with comparative sequence analysis for predicting protein function because of known error margins for high-throughput computational methods. Bork et al also indicates that one of the causes of this inaccuracy is that the quality of data available is still insufficient, especially data relating to protein function. Furthermore, Bork et al teaches that protein function is context dependent, and both molecular and cellular aspects must be considered (pg 398). Smith et al. indicates that there are numerous cases in which proteins of very different functions are homologous (pg 1222, third col, last parg). In addition, Brenner teaches the difficulty of accurately inferring function from homology and clearly states that most homologs must have different molecular and cellular functions (pg 132, col 2, parg 2). Examples, of pitfalls associated with comparative sequence analysis for predicting function, are shown by Broun et al, 1998 and Van de Loo et al, 1995. Van de Loo et al. teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* where found to

be hydroxylases, once tested for activity. Broun et al. teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase.

At the time of filing of the instant application, the sequence having highest homology with SEQ ID NO: 1 was the polynucleotide of Hillier et al, 1996 (Genbank Acc# AA179499), which has 100% identity with residues 68-337. The function of the polynucleotide of Hillier, and the polypeptide encoded thereby, is not known. However, the polynucleotide of Hillier has 98% identity with a polynucleotide taught by Zheng et al, 1990, which encodes the BTF3b transcription factor. Homology of SEQ ID NO: 1 with the polynucleotides of Hillier et al and Zheng et al teaches away from Appellant's presumed assertion that SEQ ID NO: 1 encodes a myosin light chain, a myosin light chain kinase, or a titin-like protein. Furthermore, SEQ ID NO: 2 has no detectable homology with myosin light chain or myosin light chain kinase and only 11.6% identity with human cardiac titin (Musco et al 1995). In view of the unpredictability of annotating function based on sequence homology as well as the low sequence homology between the polynucleotides/polypeptide of the instant application and polynucleotides/polypeptides having myosin light chain, myosin light chain kinase, or titin-like function as well as the homology of the instant polynucleotide to a polynucleotide encoding a protein with wholly different function (Zeng et al), one of skill in the art cannot reasonably conclude that the asserted function for the polypeptide encoded by the claimed polynucleotides is that of myosin light chain, myosin light chain kinase, or a titin-like structural protein without additional supporting evidence such as, an indication of which are the critical structural elements present in the claimed polynucleotides that are characteristic of other polynucleotides encoding myosin light

chain, myosin light chain kinase, or titin, or experimental evidence of the claimed function. In the instant case, the specification fails to provide any information or experimental evidence that would support Appellant's alleged asserted biological function.

In addition, even if one assumes that the asserted function for the polypeptide encoded by the claimed polynucleotides is that of myosin light chain, myosin light chain kinase, or a titin-like protein, the specification fails to disclose sufficient information to conclude that there is a substantial and specific utility associated with the "myosin light chain, myosin light chain kinase, or a titin-like" polynucleotide/polypeptide of the instant invention. The specification discloses that, in general, proteins are known to provide structural and mechanical scaffolding, serve as recognition markers, mediate signal transduction, and mediate translocation of molecules through the lipid bilayer (pg 1, parg 2). The specification further discloses that functional equivalents for the polypeptide of SEQ ID NO: 2 would have "the ability to bind and cleave a substrate of NHP [said polypeptide], or the ability to effect an identical or complementary downstream pathway, or a change in cellular metabolism (e.g., proteolytic activity, ion flux, tyrosine phosphorylation etc.)". Such a diverse list of possible activities for what the function of the protein set forth by SEQ ID NO: 2 might be does not disclose what the function is, i.e. what does one use a myosin light chain, myosin light chain kinase, or titin-like protein for?

The specification also asserts that the claimed polynucleotides can be used for identification of the coding sequence and mapping of polynucleotides to a particular chromosome (page 2, lines 31-33); to screen libraries, isolate clones, and prepare cloning and sequenceing templates (pg 5, lines 29-31); in microarrays, or other assays; to screen genetic material from patients; identification of mutations associated with SEQ ID NO: 1; in

hybridization assays; for analysis of expression patterns; for identification of molecular targets; and for identification of disease-related mutations (pgs 6-8); and to study protein evolution (pg 16, line 27). These utilities are not considered substantial and specific for the following reasons. The specification fails to disclose sufficient information in regard to the biological significance or further characterization of the claimed polynucleotides and the proteins encoded thereby, which would be necessary for an artisan to know how to use the claimed polynucleotides. Such as: (1) the biochemical activity of the polypeptide being encoded by the claimed polynucleotides, (2) the cellular processes or pathways in which the recited protein is involved, (3) the molecular interactions associated with the recited protein, or (4) any diseases linked to mutation/polymorphism of the recited polynucleotides and encoded proteins, such that a specific use for the claimed polynucleotides would be apparent. If information in regard to the biological role of the claimed invention were to be presented, several utilities could be apparent for the claimed polypeptide, such as purification of regulatory factors or diagnostic identification of diseases due to mutation of said protein; however, these utilities require additional information, which is not presented by the specification. As known in the art and admitted by Appellants in the specification, proteins are active in many different biological processes (pg 1, lines 21-24). Since, the cellular function of the recited protein, the biological processes associated with said protein, and any diseases due to mutation of said protein are all unknown, the utilities recited in the specification are not substantial, as they will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The instant situation is analogous to the lack of substantial utility examples provided by MPEP § 2107.01 in that basic research is

required to study the properties of the claimed polynucleotides and the corresponding polypeptide as well as the mechanisms in which the claimed polynucleotides are involved. In addition, while one could argue that some of the recited uses are specific, such as being a probe to be used in microarrays or in mapping of nucleotides in a particular chromosome, it is noted that these uses are not specific due to the fact that, all other human polynucleotides can be used as probes in microarrays or in mapping of nucleotides in the chromosome and Appellants have not provided reasons why one of skill would be motivated to use the instant polynucleotides. Since the instant specification does not disclose a credible, specific and substantial "real world" use for the polynucleotide of SEQ ID NO: 1 or any polynucleotide encoding the polypeptide of SEQ ID NO: 2, then the claimed invention, as disclosed, does not meet the requirements of 35 U.S.C. §101 as being useful.

***Claim Rejections - 35 USC §112, first paragraph***

Claims 1-3 and 6-10 are also rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. Specifically, since the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Even if the polynucleotides encoding SEQ ID NO: 2 were found to have a patentable utility and, thus, the Invention of Claims 1-3 and 6-10 was not rejected under 35 U.S.C. 101/112, first paragraph, for lack of utility, Claim 1 would still be rejected under 35 U.S.C. 112, first paragraph, for lack of enablement of the entire scope of the claimed invention for the following reasons. Claim 1 is so broad as to encompass any polynucleotide sequence comprising at least 2000 contiguous bases of SEQ ID NO: 1. Neither the specification nor the prior art teach a

skilled artisan how to use all said polynucleotides. The specification does not support the broad scope of Claim 1 because the specification does not establish: (A) the activity of any polypeptides encoded by polynucleotide sequences comprising at least 2000 contiguous bases of SEQ ID NO: 1; (B) regions of the structure of the polypeptide encoded by SEQ ID NO: 1 which may be modified without effecting the activity of said polypeptide; (C) the general tolerance of the activity of the polypeptide encoded by SEQ ID NO: 1 to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying the polypeptide encoded by SEQ ID NO: 1 with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polynucleotide sequences comprising at least 2000 contiguous bases of SEQ ID NO: 1.

Claims 7 and 10, as reciting vectors and host cells comprising the nucleic acid molecules of Claim 1 are rejected under 35 U.S.C. 112, first paragraph, for lack of enablement for the same reasons.

Likewise, even if the polynucleotides encoding SEQ ID NO: 2 were found to have patentable utility, Claim 1 would also still be rejected under 35 U.S.C. 112, first paragraph, for insufficient written description of the claimed invention. Claim 1 fails to describe any activity for any protein encoded by any species of the genus of nucleic acid molecules recited and the specification does not contain any disclosure of the functions of said genus of nucleic acid sequences. SEQ ID NO: 1 consists of 3963 bases, which encode the 1320 amino acid residues of

SEQ ID NO: 2. Thus, the genus of polynucleotides recited by Claim 1, comprising at least 2000 contiguous bases of SEQ ID NO: 1, has the potentiality of encoding many different peptide fragments with different functions or with no function. Therefore, many functionally unrelated polynucleotides are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only one species of the claimed genus, SEQ ID NO: 1, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Because the specification fails to disclose a function for the recited fragments of SEQ ID NO: 1, one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time of filing. Claims 7 and 10, as reciting vectors and host cells comprising the nucleic acid molecules of Claim 1 are rejected under 35 U.S.C. 112, first paragraph, for insufficient written description for the same reasons. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

***(11) Response to Arguments***

***A. Do Claims 1-3 and 6-10 lack a patentable utility?***

I. On page 5, paragraph 3, of the Appeal Brief, Appellants direct the reader's attention to the specification, page 11, line 9, where they assert that the specification discloses utility of the recited nucleic acid sequence as being in diagnostic assays, such as forensic analysis, and where the specific polymorphisms of said nucleic acid sequence are disclosed. In this context, Appellants argue that forensic analysis is undoubtedly a "real world" utility and, as such, the presently claimed sequences must be useful. Appellants further argue that (1) the use

of the recited nucleic acid molecules in forensics, is not potential, as they can be used without any additional research and (2) that, just because polymorphisms are common, until a polymorphic marker is actually described, it cannot be used in forensic analysis.

Reply: The specification fails to specifically assert a utility for the recited polynucleotide in forensic analysis. Even if the specification did make such an assertion, use of the recited nucleic acid molecules in forensics would not satisfy the requirement for utility under 35 U.S.C. 101. The presence of polymorphisms in human DNA is well established (Marth et al, 2001) and single nucleotide polymorphisms occur approximately once every 100 to 300 bases (NCBI, 2000). Thus, virtually any locus on a human chromosome will exhibit one or more polymorphisms, which could be used in forensic analysis. Use of the recited polynucleotide in forensics would not constitute a "real world use" as, Applicants have not identified any particular reason for analysis of the particular polymorphisms disclosed or any particular benefit that would derive from analysis of said polymorphisms. In other words, based on Appellant's disclosure, one of skill in the art would not be motivated to use the recited nucleic acid molecules in forensic analysis.

II. The Examiner is clearly confusing the requirement for a specific utility with the requirement for a unique utility. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, as the utility of each of these compositions is applicable to the broad class in which each of these compositions falls.

Reply: Appellants have never been asked to identity a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, Appellants have been required to

identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695 (An invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form.). An invention certainly can have a utility that is shared by other compound or compositions. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. So while, a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101. Here, Appellants state that the claimed polynucleotides can be used as a polymorphic marker in forensic analysis. However, any observed results of the presence or absence of the claimed polymorphism would have no meaning without additional knowledge of what the significance of this sequence variation is. The specification in effect discloses that the claimed products include a polymorphic site and leaves those of skill in the art will figure out what to do with it. This utility is not substantial; it does not provide a specific benefit in currently available form.

III. Appellants specifically emphasize a statement of *In re Brana,* which reads "Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development". In Appellant's opinion, the need for experimentation does not render the claimed invention unpatentable and they state that a considerable amount of experimentation is permissible so long as such experimentation is routinely practiced in the art. Appellants further argue that according to *In re Wands*, a patent need not disclose what is well known in the art.

Reply: While it is agreed that routine experimentation does not render an invention

unpatentable, it is noted that in the instant case, the utility rejection was not applied to the claimed invention because some routine experimentation is required to practice the claimed invention. Instead, the utility rejection was applied due to the lack of information as to the utility/biological function of the recited polynucleotides, as already discussed. The specification fails to disclose information in regard to the biological significance and further characterization of the claimed polynucleotides and the protein encoded thereby, which would be necessary for an artisan to know how to use the claimed polynucleotide. Such as: (1) the protein being encoded by the claimed polynucleotides (i.e., a specific transcription factor, kinase, protease, binding protein, cytoskeletal protein, receptor, or hormone), (2) substrates acted upon by the encoded protein, (3) the biological processes or pathways in which the encoded protein are involved, (4) the specific interactions the encoded protein is involved in (i.e. specific binding, enzymatic, structural, and signaling proteins), and (5) how mutation or polymorphism of the encoded protein affects a specific cellular function or is a cause for a specific disease. As known in the art, polynucleotides encode a wide variety of polypeptides with diverse functions. Since, the cellular function of the instant protein and the biochemical and pathological processes associated with the instant protein are all unknown, further research is required to identify or reasonably confirm a "real world" context of use (Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966)). In view of the extremely large amount of information unknown in regard to the claimed invention, it is not reasonable for one of skill in the art to conclude that the additional research required to practice the claimed invention is merely routine. In regard to *In re Wands*, while it is agreed that one need not to disclose what is well known in the art, it is noted that neither the specification nor the state of the art describe or provide any information as

to the actual biological function of the polypeptide encoded by the claimed polynucleotides other than to indicate that the polypeptide of the instant invention is a myosin light chain, myosin light chain kinase, or titin-like protein. As previously explained, the alleged assertion that the function of the recited polypeptide as a myosin light chain, myosin light chain kinase, or titin-like protein is not credible. Furthermore, by itself, said alleged assertion is insufficient to provide the skilled artisan with the knowledge of how to use the claimed polynucleotides or the polypeptides encoded thereby. Since, information which would enable one of skill in the art to practice the claimed invention is not known in the art, it is the specification which must provide the necessary information to enable the skilled artisan to practice the claimed invention.

IV. A statement of utility in the specification must be accepted, absent reasons why one of skill in the art would have reason to doubt the objective truth of such statement.

Reply: The reasons why one of skill in the art would doubt the statements of utility found in the instant specification are described in detail above, for the rejection of Claims 1-3 and 6-10 under 35 U.S.C. 101. In brief, said reasons include the following. There is no experimental evidence to support the assertion that the claimed polynucleotides encode a polypeptide having the function of myosin light chain, myosin light chain kinase, or titin. The specification does not discuss what use a myosin light chain, myosin light chain kinase, or titin protein can be put to. Said alleged functions for the claimed polynucleotides have been determined solely on the basis of structural similarity; however, at the time of filing, SEQ ID NO: 1 showed highest homology with a polynucleotide similar to a sequence encoding a transcription factor, not myosin light chain, myosin light chain kinase, or titin. Thus, in view of the unpredictability of annotating function based on sequence homology, as well as the low

sequence homology between SEQ ID NO: 2 and myosin light chain, myosin light chain kinase, and titin, one of skill in the art cannot reasonably conclude that, absent additional supporting evidence, the function for the polypeptide encoded by the claimed polynucleotides is that of myosin light chain, myosin light chain kinase, or a titin-like structural protein, even if one knew what such functions were.

V. Appellants point out that a sequence sharing nearly 100% identity at the protein level with SEQ ID NO: 2 has been identified by Bang et al, 2001, as human myopalladin (pg 10, parg 2). Appellants assert that the specification discloses that the recited polynucleotides encode "structural proteins", specifically "muscle proteins", and more specifically a "titin-like protein". It is stated that titin is well known in the art. Appellants conclude that, the function of the presently claimed sequence as a muscle structural protein was clearly asserted in the specification as originally filed, which is all that is required to satisfy the requirements of 35 U.S. 101. It is further stated that the teachings of Bang et al merely confirm Appellant's assertion and that, given said teachings and the disclosure of the specification, one of skill in the art would believe that the protein of SEQ ID NO: 2 is a muscle structural protein.

Reply: Any use of the teachings of Bang et al to establish the function of the protein set forth by SEQ ID NO: 2, without an assertion in the specification that said protein has the functional characteristics of myopalladin, including tethering nebulin and nebulette with α-actinin and regulation of Z-line architecture, represents only hind-sight reasoning. The specification fails to disclose that the protein of SEQ ID NO: 2 has said functional characteristics of myopalladin.

As described above for the rejection of Claims 1-3 and 6-10 under 35 U.S.C 101, disclosure that the claimed polynucleotides encode "proteins that share sequence similarity with mammalian membrane and structural proteins" and that "the novel human proteins described... share structural similarity with *inter alia*, mammalian muscle proteins" does not constitute an assertion of function. While structural similarity may indicate functional similarity, this is not always the case. Appellant's specification does not even go so far as to assert functional similarity. It states only that, the protein encoded by the claimed polynucleotide is structurally similar. Furthermore, even if the specification had asserted a function for the polypeptide of SEQ ID NO: 2 as a structural protein of muscle, said assertion would not teach one of skill in the art how to use said polypeptide or any polynucleotide encoding it. The genus of proteins encompassed by "structural proteins of muscle" is a large and variable genus with diverse functions. For example, titin connects thick myosin filaments to Z discs in the sarcomere (Smith et al, 2000; pg 649), while myosin light chain is an ATPase that occurs in the contractile apparatus and mediates contraction of skeletal muscle (Smith et al, 2000; pg 437). Since the specification fails to teach the function of the recited polypeptide in any specific biochemical processes, further experimentation is required to determine the function. Said experimentation, which is undue, is left to the public to perform.

VI. Appellants point out that the association of a nucleotide sequence with a particular type of disease is not the standard for patentability under 35 U.S.C 101 and that the Federal Circuit admonished the P.T.O. for confusing the requirement under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption.

Reply: While it is agreed that FDA approval is not a requirement for finding a compound patentably useful, it is noted that in the instant case, the utility rejection was not applied to the claimed invention because it failed to comply with government requirements to market the invention for human consumption. Instead, the utility rejection was applied due to the lack of information as to its biological function, as already discussed above.

VII. Appellants argue that, although only one credible assertion of utility is needed to meet the requirements of 35 U.S.C. 101, the present nucleotide sequences also have the following utilities.

(A) Utility in assessing gene expression patterns using high-throughput DNA chips and that such DNA chips clearly have utility, as evidenced by hundreds of issued U.S. Patents (pg 12, lines 4-11). Appellants point out that nucleic acid sequences are commonly used in gene chip applications without any information regarding the function of the encoded protein. Appellants further argue the following. Such cDNA chips clearly have utility, as evidenced by hundreds of issued US patents. Evidence of the real world substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. One such company, (Rosetta Inpharmatics) was viewed to have such "real world" value that, it was acquired by a large pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences and that said sequences have utility, given the wide spread utility of such "gene chip" methods.

Reply: It is agreed that the use of polynucleotides in DNA chips (microarrays) is widespread and that the claimed polynucleotides can be attached to DNA chips. However, as indicated by the Examiner in previous Office Actions, for the claimed polynucleotides to be specifically useful in such application, one would require some knowledge or guidance as to the biological role of the polypeptide encoded by such polynucleotides to effectively use the information gathered in tracking the expression patterns of such polynucleotides. The reduction or increase in expression of a polynucleotide is meaningless unless one can link changes in expression with some biological function. For example, if one were to use the claimed polynucleotides in assays which would lead to the discovery of drugs of a specific condition, such as an assay which uses a DNA chip to evaluate expression patterns upon exposure to a test compound, one needs to know which diseases and/or biological functions are associated with the expression of such polynucleotides. Otherwise, one of skill in the art would have to carry out further experimentation to determine which are the conditions (i.e. diseases) and/or biological functions associated with the claimed polynucleotides. Appellant's asserted utility of the claimed polynucleotides as specific markers which are targets for discovering drugs associated with human disease is not a specific and substantial utility since the specification is silent in regard to (1) the conditions and/or biological functions which are associated with the expression of the claimed polynucleotides, (2) whether increase or decrease in expression correlates with disease, and (3) which levels of increase or decrease in expression of the claimed polynucleotides are indicative of the presence or absence of a disease. This is analogous to the examples provided by MPEP § 2107.01 in regard to what constitutes carrying out further research to identify or reasonably confirm a "real world" context of use since, basic research is

required to determine the properties or the mechanisms in which the claimed product is involved. The Examiner acknowledges the hundreds of issued patents in regard to DNA chips; however, it is noted that the instant claims are not drawn to methods of use of DNA chips or to DNA chips (microarrays) but rather to specific polynucleotides. Furthermore, the asserted use of the intant polynucleotides in DNA chips is not specific since, as Appellants have stated, many other polynucleotides including those in the public domain can and are used in DNA chips. In regard to the argument that the claimed polynucleotides can be used as specific markers of the human genome and specifically chromosome 10, it is noted that there is no disclosure in the specification as to how the claimed invention is a specific marker of the human genome or that the claimed polynucleotide is a marker of chromosome 10. Furthermore, the specification fails to teach why a marker of human chromosome 10 would be useful, i.e., as a marker of specific chromosome abnormalities etc. This situation is analogous to the examples provided in MPEP § 2107.01 in regard to what constitute a non-specific utility since, as stated MPEP § 2107.01 "a specific utility is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to a broad class of inventions". Therefore, in view of the lack of information as to the biological function and/or condition associated with the expression of the claimed polynucleotides or how the claimed invention is a specific marker of the human genome, it is unclear how one of skill in the art can reasonably conclude that the asserted use of the claimed polynucleotides in DNA chips or as a human genome marker is a specific and substantial utility.

(B) Appellants state that the recited polynucleotides have a specific utility in the identification of coding sequence and in determining the genomic structure of the protein coding

regions of the corresponding human chromosome. Appellants further argue the following. That said utility is evidenced by the fact that SEQ1DNO:1 can be used to map the 19 coding exons on chromosome 10 (present within three overlapping chromosome 10 clones; GenBankAccession Numbers AC024258, A1.,512429 and AC016395). Appellants remind the Board that only a minor percentage (2-4%) of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (e.g., showing which sequences are transcribed, spliced, and polyadenylated), which specifically define the portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (i.e., the described sequences are useful for functionally defining exon splice-junctions). It is well known that intron/exon boundaries are mutational hot spots, and thus the identification of the actual splice sites is of great utility to the skilled artisan. Such biologically validated splice junctions are superior to splice junctions predicted from genomic sequence alone, and, as detailed in the specification, sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used in designing primers for use in amplification assays to detect mutations which can be used in diagnostics and pharmacogenomics. Appellants respectfully submit that the practical scientific value of biologically validated, expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts.

Reply: While it is agreed that the claimed polynucleotides can be used in detecting the particular locus (i.e. position in the chromosome at which the gene resides) of the human genome

where the gene encoding the polypeptide of SEQ ID NO: 2 is located and to map the coding exons in said locus, such use is not considered specific for the following reasons. As known in the art, any human polynucleotide that encodes a protein can be used to detect the particular locus of the corresponding gene and to map the exons within the locus. The specification fails to disclose the usefulness of said information regarding the claimed polynucleotides. For example, the specification fails to identify any intron/exon border regions which is involved in any disease process etc. In regard to the use of the claimed polynucleotides to design primers for use in amplifications assays to detect mutations, within the claimed polynucleotides, which can be used in diagnostics and pharmacogenomics, it is noted that this use is not specific since, many other polynucleotides which encode proteins, as indicated above, can be used in a similar way. In addition, it is noted that there is no disclosure in the specification as to any diseases, conditions or biological changes associated with mutations in the structure of the gene encoding the polypeptide of SEQ ID NO: 2, which would motivate one of skill in the art to use the claimed polynucleotides as probes to detect mutations in that specific locus.

VIII. Appellants argue that, the Federal Circuit has clearly stated "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." Appellants cite *Juicy Whip Inc. v. Orange Bang Inc, Brooktree Corp. v. Advanced Micro Devices, Inc, Cross v. Izuka, State Street Bank & Trust Co. v. Signature Financial Group Inc,* and *Diamond vs. Chakrabarty.*

Appellants further argue that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or

particular guidelines for patent examination set forth by the USPTO and that, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. They state that numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines (U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281, 6,340,583), none of which contains examples of the "real-world" utilities that the Examiner seems to be requiring.

Reply: The Examiner acknowledges the numerous cases cited by Appellants, wherein issues in regard to 35 USC § 101 were examined. It is noted however that only *Cross v. Iizuka* is considered relevant to the instant discussion since the inventions in that case are chemical compounds. In *Juicy Whip Inc. v. Orange Bang, Inc.,* the issue of utility was discussed in regard to a juice dispenser, *in Brooktree Corp. v. Advanced Micro Devices, Inc.,* the issue of utility was discussed in regard to a digital to analog conversion circuitry, and in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.,* the issue of utility was discussed in regard to a business method.

In *Cross v Iizuka*, the issues which the Federal Circuit had to examined were whether the Board erred in finding that the utility disclosed in the Japanese priority application by Iizuka was sufficient to meet the practical utility requirement of 35 U.S.C. §101 and whether the Board erred in finding that the Japanese priority application contained sufficient disclosure to satisfy the enablement, i.e., how-to-use, requirement of 35 U.S.C. § 112. The PTO, the Board of Patent Appeals and Interferences, and the Federal Circuit found that the claimed imidazole derivative compounds had practical *in vitro* utility since, in addition to the disclosure of the structure of the claimed imidazole derivative compounds, there was experimental evidence of the strong

inhibition of thromboxane synthetase by these imidazole derivatives in human and bovine microsomes. Thromboxane synthetase is an enzyme which leads to the formation of thromboxane A2, which at the time the applications of Cross and Iizuka were filed, was postulated to be a causal factor in platelet aggregation which, in turn, is known to be associated with platelet thrombosis, pulmonary vasoconstriction or vasospasm, inflammation, hypertension, and collagen-induced thrombosis. In contrast, the instant application discloses the structure of the claimed polynucleotides and no biological characterization of the polypeptide encoded by the claimed polynucleotide other than to state that, based on sequence homology, it appears to be a myosin light chain, myosin light chain kinase, or titin-like protein. For the reasons indicated above, even if one assumes that the polypeptide encoded by the claimed polynucleotides is a myosin light chain, myosin light chain kinase, or titin-like protein, the specification fails to provide sufficient information for one of skill in the art to know how to use the claimed invention. The specification is silent in regard to (1) the biochemical activity of the polypeptide being encoded by the claimed polynucleotides, (2) the biological processes or pathways in which the recited protein is involved, (3) the specific molecular interactions associated with the recited protein, or (4) any diseases linked to mutation of the recited polynucleotides and encoded proteins, such that a specific use for the claimed polynucleotides would be apparent. While one of skill in the art can reasonably conclude that the chemical compounds of Iizuka had a credible, specific and substantial utility, i.e. the imidazole derivative compounds inhibit an specific enzyme, thromboxane synthetase, in human and bovine microsomes, a skilled artisan cannot reasonably conclude that the claimed polynucleotides have a specific and substantial, or even credible utility in view of the evidence presented.

Appellants are reminded that the Examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the Examiner has no authority to disregard such guidelines or to apply her own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were promulgated by the PTO in accordance with all applicable case law and thus are believed to be consistent therewith. While the Examiner acknowledges the US patents of Exhibits K, L, M and N, as indicated in previous Office Action Paper No. 11 (Final Rejection), mailed on 5/7/2002 and Paper No. 13 (Advisory Action), mailed on 7/30/2002, each application is examined on its own merits according to the current guidelines of examination as set forth by the USPTO and a discussion on the utility of any polynucleotide claimed in such patents would require a detailed review of the record of each individual case, which would be improper herein. Finally, Appellants are further reminded that the Examiner has no authority to comment in regard to the legality of the new utility guidelines or the MPEP as set forth by the USPTO.

***B. Are Claims 1-3 and 6-10 unusable due to a lack of patentable utility?***

On page 17, paragraph 3, of the Brief, Appellants indicate that arguments detailed in section VIII(A) of the Brief are incorporated by reference due to the fact that it has been determined by the courts that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph have the same basis. Appellants argue that since Claims 1-3 and 6-10 have been shown to have a "specific, substantial and credible utility" as indicated in section VIII(A), the present rejections under 35 USC 112, first paragraph cannot stand. Thus, as indicated by Appellants, a rejection under § 112, first paragraph, may be

affirmed on the same basis as a lack of utility rejection under § 101. *See, e.g., In re Swartz*, 56 USPQ2d 1703 (Fed. Cir. 2000); *In re Kirk*, 153 USPQ 48 (CCPA 1967).

***C. Does Claim 1 lack sufficient written description?***

In support of their request for withdrawal of the rejection of Claim 1 under 35U.S.C. § 112, for insufficient written description, Appellants provide the following arguments (pgs 18-20). The Examiner seems to be requiring a complete and exact description of every member of the claimed genus and Appellants point out that this is not the standard for compliance with 35 U.S.C. 112, first paragraph. Appellants further point out that there is no requirement whatsoever that novel fragments of a novel sequence have the exact same function as the full length sequence in order to be patented. If this were the case, hundreds, if not thousands, of issued U.S. Patents would be instantly invalidated. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19USPQ2d 111 (Fed. Cir. 1991) held that "applicant must convey with reasonable clarity to those skill in the art that, as of the filing date sought, he or she was in possession of the invention". As apposed to the situation set forth in *Regents of Univ. of California v. Eli Lilly and Co.* and *Fiers v. Revel*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features- a chemical formula, i.e., the sequence itself. (All Appellant's emphasis.)

Reply: It is acknowledged that 35 U.S.C. 112, first paragraph requires the subject matter of the recited invention be described in the specification only in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and that, a complete and exact description of every member of the claimed genus is not required. It is also acknowledged that Claim 1 provides

sufficient structural written description in reciting: nucleic acid molecules comprising at least 2000 contiguous bases of SEQ ID NO: 1. A skilled artisan would known how to make said nucleic acid molecules. However, in addition to the requirement for structural written description, 35 U.S.C. 112, first paragraph, also requires the functional subject matter of the recited invention be described, as said paragraph states that the written description should be "in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains or with which it is most nearly connected to make and use the same...". Said requirement for functional written description of the claimed genus is not met by either Claim 1 or the specification as, Claim 1 does not recite a function for any fragment of SEQ ID NO: 1 and the specification fails to disclose a inherent function for all fragments within the claimed genus. Appellants point out that, for a patent to be issued, there is no requirement that fragments of a sequence have the same function as the full-length sequence, is acknowledged. However, in order for one of skill in the art to be convinced that Appellants were in possession of the genus of the claim, there is a requirement that the claims or specification disclose a function for the genus of fragments claimed. As the genus is diverse in functional characteristics, a description of the characteristics of only a single species within said genus is insufficient as the single species is not representative of the genus as a whole.

Appellants argue that the current claims are fundamentally different from the types of claims the court has found to lack sufficient written description. The current claims recite the genus of polypeptides claimed in strictly structural terms, while the claims found to lack written description in cases such as *Fiers v. Revel* and *University of California v. Eli Lilly and Co.* defined the claimed genus in strictly functional terms. The Examiner acknowledges that, the

current claims differ from those held by the court to lack sufficient written description as discussed in the written description guidelines. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that, the adequately described species are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicants was in possession of the necessary common attributes of features of the elements possessed by the members of the genus in view of the species disclosed. As discussed above, such attributes and features include both the structure and function. For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species, cannot be achieved by disclosing only one species within the genus. In the instant case, the claimed genera of Claims 1, 7, and 10 includes species, which vary widely in function. A nucleic acid molecule comprising at least 2000 contiguous bases of SEQ ID NO: 1 might encode a protein that binds to the nebulin SH3 domain, a protein that binds to α-actinin, or a protein that interacts with the sarcomeric cardiac ankyrin repeat protein, as for the domains of myopalladin (Bang et al, 2001) or might encode a protein with no function at all. As such, neither the description of the structure and function of SEQ ID

NO: 1 nor the disclosure of solely structural features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

Therefore, for reasons set forth above, Appellants arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the prima facie case of lack of utility or insufficient written description and it is believed that the rejections should be sustained.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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